Complete Summary

GUIDELINE TITLE

Multiple myeloma (MM).

BIBLIOGRAPHIC SOURCE(S)

Vilpo J. Multiple myeloma (MM). In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2004 Jun 14 [various]. [12 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Finnish Medical Society Duodecim. Multiple myeloma (MM). Helsinki, Finland: Duodecim Medical Publications Ltd.; 2001 Dec 27. Various p.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Multiple myeloma (MM)

GUIDELINE CATEGORY

Diagnosis
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Oncology

INTENDED USERS

Health Care Providers
Physicians

GUIDELINE OBJECTIVE(S)

Evidence-Based Medicine Guidelines collects, summarizes, and updates the core clinical knowledge essential in general practice. The guidelines also describe the scientific evidence underlying the given recommendations.

TARGET POPULATION

- Patients with multiple myeloma (MM)
- Patients requiring evaluation for possible multiple myeloma

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Measures to distinguish between early cases of multiple myeloma (MM) and benign paraproteinaemias, especially monoclonal gammopathy with undetermined significance (MGUS).
2. Differential diagnosis
3. Assessment of clinical picture
4. Basic examinations: blood picture, serum calcium, potassium, natrium and creatinine, and erythrocyte sedimentation rate (ESR); bone marrow examination; serum and urine protein electrophoresis
5. Additional investigations when multiple myeloma is likely:
    - X-ray (skull, thorax/ribs, backbone, scapulae, pelvis and long bones of the extremities)
    - Serum/plasma total protein, albumin, potassium, sodium, calcium, ionised calcium, creatinine, urate and immunoglobulins (IgG, IgA, IgM)
    - Identification of M component heavy and light chains by immunofixation or by other means
    - NOTE: Magnetic resonance imaging is more sensitive than radiography, but is seldom indicated in basic diagnosis.

Treatment; Management

1. Follow-up, including assessment of:
    - The amount of M component (serum and/or urine)
    - The blood picture (reflects the degree of bone marrow infiltrates)
    - General condition and symptoms, infections and (bone) pains
    - Osteolytic lesions (X-ray)
    - Renal function, hypercalcaemia and blood picture
2. Chemotherapy

- Vincristine, adriamycin, and dexamethasone (VAD) or similar combinations when stem cell transplantation is considered or a rapid response is needed.
- MP therapy (a combination of melphalan and prednisolone) especially for patients over 70 years of age and also for younger patients if stem cell transplantation is not considered
- Refractory cases
    - VAD (vincristine, adriamycin and dexamethasone)
    - MOCCA (vincristine, cyclophosphamide, lomustine, melphalan and methylprednisolone), high-dose melphalan or other cytostatics
    - Thalidomide
    - Dexamethasone
- Interferon

3. Supportive therapy
    - Maintenance of fluid and electrolyte balance
    - Treatment of hypercalcaemia
    - Treatment of infections
    - Maintenance of mobility in order to prevent osteoporosis and pathological fractures
    - Treatment of anaemia and thrombocytopenia, if necessary
4. Stem cell transplantation (autologous or allogeneic) as indicated

MAJOR OUTCOMES CONSIDERED

- Signs and symptoms of multiple myeloma
- Complications of multiple myeloma, including pathological vertebral fractures
- Survival (lifetime and progression-free)
- Mortality

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The evidence reviewed was collected from the Cochrane database of systematic reviews and the Database of Abstracts of Reviews of Effectiveness (DARE). In addition, the Cochrane Library and medical journals were searched specifically for original publications.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

A. Strong research-based evidence. Multiple relevant, high-quality scientific studies with homogeneous results.
B. Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies.
C. Limited research-based evidence. At least one adequate scientific study.
D. No research-based evidence. Expert panel evaluation of other information.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of evidence [A-D] supporting the recommendations are defined at the end of the "Major Recommendations" field.

Aim

To recognize symptoms that require early intervention

Pathology

- Multiple myeloma (MM) is a clonal bone marrow proliferation of mature B cells (plasma cells) characterized by a monoclonal immunoglobulin fraction (M component) in the serum or sometimes only in urine protein electrophoresis.
- Benign disease forms (monoclonal gammopathy with unknown significance [MGUS] and benign paraproteinaemia) are about 100 times more common than myeloma.

Epidemiology

- Approximately 3 to 4 new cases/100,000/year
- Diagnosis is usually made at the age of 50 to 70 years, rarely before the age of 40 years.
- No sex differences

Aetiology

- In individual patients aetiology remains unknown.
- Ionising radiation slightly increases the risk.

Diagnosis

- The main diagnostic difficulty is to make a distinction between early cases of MM and "benign" paraproteinaemias, especially MGUS.

Criteria for Diagnosis of Multiple Myeloma (World Health Organization [WHO] Classification)

A. The diagnosis of multiple myeloma requires one main criterion and at least one additional criterion OR three additional criteria, which include C1 and C2. In addition, the disease has to be symptomatic and progressive.
B. Main criteria
    1. Bone marrow plasmacytosis (> 30%)
    2. Plasmacytoma in biopsy
    3. M component
        - Serum/plasma: Immunoglobulin G (IgG) >35 g/L, IgA >20 g/L
        - Urine: >1 g/24 h
C. Additional criteria
    1. Bone marrow plasmacytosis (10–30%)
    2. M component (smaller than in point B3)
    3. Osteolytic lesions
    4. Decrease of polyclonal immunoglobulins in serum
        - IgG <6 g/L
        - IgA <1 g/L
        - IgM <0.5 g/L

Differential Diagnostics

- MGUS (plasma cells in bone marrow <10%; IgG <35 g/L or IgA <20 g/L, no osteolytic foci, no symptoms)
- Waldenström's macroglobulinaemia (See Finnish Medical Society Duodecim guideline "Waldenström's macroglobulinaemia [WM]")
- Lymphomas with an M component in some cases
- Other rare diseases where there is an M component

Clinical Picture

- Often:
    - Osteolytic lesions and bone pains
    - Mild anaemia, hypercalcaemia, hyperuricaemia
    - Renal insufficiency
- Rarely:
    - Hyperviscosity syndrome (IgA myeloma)

Typical Laboratory Findings

- Increased erythrocyte sedimentation rate (ESR) (not in light-chain myeloma)
- M component in serum and/or urine
- Decreased haemoglobin level, often also leuco- and thrombocytopenia
- Malignant plasma cell infiltrates in the bone marrow
- Osteolytic lesion in bone radiography
- Often increased serum urate and calcium but diminished albumin concentration

Basic Examinations

- Blood picture, serum calcium, potassium, natrium and creatinine, and ESR
- Bone marrow examination
- Serum and urine protein electrophoresis (M component can be found in urine in only 10 to 20% of MM patients)

Additional Investigations when MM is Likely

- Radiography (skull, thorax/ribs, vertebrae, scapulae, pelvis and long bones of the extremities)
- Serum/plasma total protein, albumin, potassium, sodium, calcium, ionised calcium, creatinine, urate and immunoglobulins (IgG, IgA, IgM)
- Identification of M component heavy and light chains by immunofixation or by other means
- Magnetic resonance imaging is more sensitive than radiography, but is seldom indicated in basic diagnosis.

Complications Requiring Attention Preferably Within 24 Hours (Particularly in New Patients)

- Sepsis or pneumonia (intravenous broad-spectrum antibiotics)
- Renal insufficiency (dialysis or haemofiltration)

- Hyperviscosity (plasmapheresis)
- Hypercalcaemia (fluid replacement, bisphosphonates, steroids)
- Spinal cord compression (surgical decompression, radiotherapy?)
- Pathological fractures (pain medication, stabilization)
- Vertebral compression (orthopaedic treatment)

Disease Progression and Prognosis

- With traditional therapies, median life expectancy at diagnosis is about 3.5 to 4 years and somewhat longer with more intensive treatments. Marked individual variation exists.
- Myeloma cells become gradually resistant to chemotherapy.
- Myeloma cell infiltrates occupy the bone marrow causing anaemia, thrombocytopenia, and leucopenia.
- Infections, haemorrhages and renal insufficiency are frequent complications.

Follow-up and Treatment

- If the patient is symptomless, no chemotherapy is usually given, as it does not improve the patient´s well being or prolong life.
- Symptomatic patients are treated actively.

In Follow-up, Attention is Paid to:

- The amount of M component (serum and/or urine)
- The blood picture (reflects the degree of bone marrow infiltrates)
- General condition and symptoms, infections and (bone) pains
- Osteolytic lesions (radiography)
- Renal function and hypercalcaemia

Chemotherapy

- According to instructions given by a haematologist or a specialist in internal medicine who is familiar with the treatment of haematological diseases: the aim is intensive therapy and two successive autologous stem cell transplantations (patients under 70 years).
- VAD (vincristine, adriamycin and dexamethasone) or similar combinations when stem cell transplantation is considered or a rapid response is needed.
- MP therapy (a combination of melphalan and prednisolone) especially for patients over 70 years of age and also for younger patients if stem cell transplantation is not considered
- Refractory cases
    - Vincristine, adriamycin, and dexamethasone (VAD)
    - Vincristine, cyclophosphamide, lomustine, melphalan, and methylprednisolone (MOCCA), high-dose melphalan, or other cytostatics
    - Thalidomide
    - Dexamethasone
- Interferon may be tried (Trippoli et al., 1997; DARE-971500, 1999) [B] especially for maintaining an otherwise reached good response.

Supportive Therapy Includes:

- Maintenance of fluid and electrolyte balance (to prevent renal failure)
- Treatment of hypercalcaemia
- Treatment of infections
- Maintenance of mobility in order to prevent osteoporosis and pathological fractures
- If necessary, treatment of anaemia and thrombocytopenia

Stem Cell Transplantation

- Autologous stem cell transplantation is used increasingly and is often the first-line treatment for patients over 70 years of age (Johnson et al., 1998; DARE-989011, 2000) [C].
- Allogeneic stem cell transplantation is also used increasingly, but it is still possible only for few patients.

Related Evidence

- Early treatment of early stage multiple myeloma appears to inhibit disease progression and reduce vertebral compression. However, early treatment may increase the risk of acute leukaemia (He et al., 2003) [B].

Definitions:

Levels of Evidence

A. Strong research-based evidence. Multiple relevant, high-quality scientific studies with homogeneous results.
B. Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies.
C. Limited research-based evidence. At least one adequate scientific study.
D. No research-based evidence. Expert panel evaluation of other information.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Concise summaries of scientific evidence attached to the individual guidelines are the unique feature of the Evidence-Based Medicine Guidelines. The evidence summaries allow the clinician to judge how well-founded the treatment

recommendations are. The type of supporting evidence is identified and graded for select recommendations (see the "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Reduction of symptoms and prevention of complications through early diagnosis and treatment

POTENTIAL HARMS

Not stated

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 Dec 27 (revised 2004 Jun 14)

GUIDELINE DEVELOPER(S)

Finnish Medical Society Duodecim - Professional Association

SOURCE(S) OF FUNDING

Finnish Medical Society Duodecim

GUIDELINE COMMITTEE

Editorial Team of EBM Guidelines

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Author: Juhani Vilpo

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

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GUIDELINE AVAILABILITY

This guideline is included in a CD-ROM titled "EBM Guidelines. Evidence-Based Medicine" available from Duodecim Medical Publications, Ltd, PO Box 713, 00101 Helsinki, Finland; e-mail: info@ebm-guidelines.com; Web site: www.ebm-guidelines.com.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on December 17, 2002. The information was verified by the guideline developer as of February 7, 2003. This NGC summary was updated by ECRI on October 5, 2004.

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